OMICS Group Conferences
Accelerating Scientific Discovery

3rd World Congress on
Cancer Science & Therapy

October 21-23, 2013 DoubleTree by Hilton Hotel San Francisco Airport, USA

Inhibitors of the histone methylase EZH2, a new anti-tumoral therapy ?

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Abstract

The identification of new therapeutic approaches capable of treating tumors resistant to current treatments (radiotherapy and chemotherapy) is a major public health issue. Among the newly emerging strategies, epigenetic therapy looks promising, especially with regard to the targeting of the methylation of histone H3 on lysine 27 (H3K27). This methylation can be unique (H3K27me1), double (H3K7me2) or triple (H3K27me3). The H3K27me1 mark is usually associated with active genes, while H3K27me3 mark is often found in silenced genes. H3K27 is methylated by a single enzyme, EZH2, which is part of PRC2 complex, and demethylated by two specific histone demethylase, called UTX and JMJD3. Recently, it has been shown that 3-deazaneplanocin A (DZNep), an inhibitor of PRC2 (Polycomb Repressive Complex 2), induces apoptosis of malignant cells but not healthy cells, opening the way for the concept of epigenetic therapy to treat tumors by inhibiting H3K27 methylation. DZNep reduces the clonogenic potential of many tumors, probably through the inhibition of EZH2 expression and the subsequent reduction of H3K27 methylation. However, this mechanism remains to be confirmed.

This lecture will address the importance of EZH2 in tumors and I will present our current research aiming to validate the concept of epigenetic therapy to treat resistant tumors, such as chondrosarcomas, by targeting the methylation of H3K27 using chemical agents, such as DZNep.

Biography

Catherine Baugé has studied cartilage biology at University of Caen. She received her PhD Degree in cellular biology in 2006. Then she joined National Cancer Institute of NIH where she studied histone demethylase functions. In 2009, she became an associated professor in France. Her current research is about role of histone methylation in tumors in focusing on chondrosarcomas. She received several research awards. She is member of several societies, and worked as reviewer for many internationally reputed journals. She has a number of publication in international journals.